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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/725,349	12/02/2003	Teresa Mujica-Fernaud	MERCK-2805	1371

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EXAMINER	
OWENS, AMELIA A	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 05/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/725,349	MUJICA-FERNAUD ET AL.	
	Examiner	Art Unit	
	Amelia A. Owens	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,11,14-16,18,21-25 and 28-34* is/are pending in the application.

4a) Of the above claim(s) *22-25 and 28-32* is/are withdrawn from consideration.

5)☒ Claim(s) *1-7,11 and 34* is/are allowed.

6)☒ Claim(s) *11,14-16,18 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 8-10,12,13,17,19,20,26,27,33 have been canceled. Claims 22-25,28-32 remain withdrawn. Claims 1-7,11,14-16,18,21,34 are pending.

2. Claim 28 is listed as canceled and withdrawn. Please clarify/correct.

3. The indicated allowability of claims 14-16 is withdrawn in view of the rejection below.

Restrictions

4. The petition regarding the restriction is noted. However, it had not been decided at the time the action was written.

Claim Rejections - 35 USC § 112

5. The rejection of claims 8-10,12,13,17,19,20,26,27,33 under 35 USC 112, 1st paragraph is dropped as the claims have been canceled.

6. Claims 11,14-16,18,21 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification @ page 35 lines 23-25 define treatment as 'prevention of diseases and treatment of pre-existing conditions'. Therefore with the recitation of 'treatment' in the claims, 'prevention of diseases' is automatically included.

The specification does not enable any physician skilled in the art of medicine, to use the invention commensurate in scope with these claims. "The [eight] factors to be considered have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. All of the factors have been considered, but only the most pertinent discussed below. The main issue is the correlation between clinical efficacy for 'treatment of pre-existing conditions' named and Applicants' assay outlined on pages 37-38 of the specification.

a) Determining if any particular claimed compound would treat any of the named diseases would require synthesis of the compound, formulation into a suitable dosage form, and subjecting it clinical trials with the number of fundamentally different recited diseases described in the specification, or to testing them in an assay known to be correlated to clinical efficacy of such treatment. This is a large quantity of experimentation. b) The direction concerning treating the named diseases is found in the specification, which merely states Applicants' intention to do so. Applicants describe formulations at page 35 line 35 thru 36 line31. Doses required to practice their invention are described page 36 lines 32-36. A range of doses is recommended. Since no 2-benzoylchromone compound has ever been used to treat any human disease, how is the skilled physician to know what dose to use for each of these different diseases? There are no guidelines for determining the doses needed to provide a positive effect *vs.* a negative effect *vs.* no effect. Are the identical doses to be used for treating these unrelated diseases? There is a VEGF receptor kinase assay described at page 37 line 31 thru 42 lie 27 - with no data. It is unclear if this assay is correlated to the named diseases. c) There is no working example of treatment of any of the named diseases in man or animals. Again, the VEGF receptor kinase assay is noted. d) The nature of the invention is clinical treatment of disease with compounds of the claims, which involves physiological activity. e) The state of the clinical arts is that tyrosine kinase receptors were just identified as potential targets for small cell lung cancer. See Jafri, Mechanisms of metastasis as related to receptor tyrosine kinase in small-cell lung cancer, PMID: 14529091 (2003). Further, it is not seen where tyrosine kinase is implicated in the treatment of rickets.

f) The artisan using Applicants invention would be a physician with a MD degree and several years of experience. g) It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 166 USPQ 18, at 24 (In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.), *Nationwide Chemical Corporation, et al. v. Wright, et al.*, 192 USPQ 95 (one skilled in chemical and biological arts cannot always reasonably predict how different chemical compounds and elements might behave under varying circumstances), *Ex parte*

Sudilovsky 21 USPQ2d 1702 (Appellant's invention concerns pharmaceutical activity. Because there is no evidence of record of analogous activity for similar compounds, the art is relatively unpredictable) *In re Wright* 27 USPQ2d 1510 (the physiological activity of RNA viruses was sufficiently unpredictable that success in developing specific avian recombinant virus vaccine was uncertain). h) The scope of the claims involves all of the many compounds of the claims as ell as the many named diseases mentioned in the claims. Thus, the scope of claims is broad.

MPEP §2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

Certain Observations

7. Claims 1-7,34 are allowed. The prior art neither teaches nor suggests the claimed compounds. In the absence of any evidence or apparent reason why the claimed compounds do no possess the disclosed utility, the allegation of utility in the specification must be accepted as correct. In re Kamal et al, 158 USPQ 320; Ex parte Krenzer, 199 USPQ 227.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amelia A. Owens whose telephone number is 571-272-0690. The examiner can normally be reached on Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Amelia A. Owens
Primary Examiner
Art Unit 1625